AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning on page 1, line 2 as follows:

The present invention is a divisional of U.S. patent application Serial No. 10/294,770 filed on November 15, 2002, now abandoned, which is a continuation in part of U.S. application no. 10/238,741 filed September 11, 2002, which is a continuation of application no. 09/356,497 filed July 19, 1999, now U.S. Patent 6,472,519, which is a divisional of U.S. application no. 08/416,711, filed August 8, 1995, now U.S. Patent 6,017,538, which was originally filed as International Application no. PCT/FR93/01024 on October 18, 1993.

Please amend the paragraph beginning on page 19, line 28 as follows:

Any ~~pharmaceutical~~ pharmaceutically acceptable vehicle can be used in the vaccine such as an adjuvant that enhances the immunogenicity of the long synthetic peptides. Examples of such adjuvants include alum, muramyl peptides and ~~Montanide~~ MONTANIDE®. MONTANIDE® are a group of oil/surfactant based adjuvants in which different surfactants are combined with either a non-metabolizable mineral oil, a metabolizable mineral oil or a mixture of the two. Other pharmaceutically acceptable vehicles include saline and the like.

Please amend the paragraph beginning on page 32, line 28 as follows:

The primary objectives were to evaluate the safety and tolerance of the subcutaneous (s.c.) administration of a long synthetic peptide (LSP) derived from MSP3, a *Plasmodium falciparum* merozoite surface antigen, as a potential malaria vaccine candidate, by comparing two adjuvant formulations (Alum *vs* ~~Montanide~~ MONTANIDE® 720) and four dosages of peptide (10 μg, 30 μg, 100 μg and 300 μg).

Please amend the paragraph beginning on page 33, line 3 as follows:

The secondary objectives were to determine the immunogenicity of LSP in the presence of adjuvant (Alum or ~~Montanide~~ MONTANIDE® 720), by measuring at day 0, 30, 60, 120, 150 and 360) the specific antibody and antibody subtype response to the MSP3 peptide, the antibody dependent cell inhibition (ADCI)) by evaluating antibody recognition of parasite antigen by direct immunofluorescence and by following the T-cell specific response to the MSP3 antigen (cell proliferation, cytokine production).

Please amend Table 2 appearing on page 33 as follows:

Table 2

Stratum	Treatment	No. of volunteers
1	10 µg LSP (~~Montanide~~ MONTANIDE® 720)	6
2	30 µg LSP (Alum)	6
	30 µg LSP (~~Montanide~~ MONTANIDE® 720)	6
3	100 µg (Alum)	6
	100 µg (~~Montanide~~ MONTANIDE® 720)	6
4	300 µg (~~Montanide~~ MONTANIDE® 720)	6

Please amend the paragraph beginning on page 35, line 6 as follows:

The overall clinical tolerance proved to be excellent, however with a trend towards enhanced reactogenicity with ~~Montanide~~ MONTANIDE® as compared to alum. There were no systemic reactions, no fever or malaise and no severe adverse events. Biological tests and haematological parameters remained all along of the study, within normal ranges. However, mild, short-lived and self-resolving local erythema occurred in some of the volunteers at the site of injection, mostly when using ~~Montanide~~ MONTANIDE® as an adjuvant and mostly

upon the second injection. This had been foreseen since it has been described with other trials relying on the use of ~~Montanide~~ MONTANIDE® and sometimes with alum.

Please amend the paragraph beginning on page 35, line 15 as follows:

Therefore, it had been decided beforehand that local reactions superior to 10 cm in diameter would lead to exclusion of the volunteers from further immunization. This criteria was revised by the clinicians who decided to exclude all reactions superior to 8 cm in diameter. The results are summarized in Table 3 below. No such reaction was seen after the first injection in any of the treated groups. After the second injection 5 occurred within the ~~Montanide~~ MONTANIDE® groups, 2 occurred after the third injection, one in the ~~Montanide~~ MONTANIDE® group and one in the alum group.

Please amend the paragraph beginning on page 35, line 23 as follows:

The reaction consisted of a local erythema at the site of injection and a degree of induration of the skin. It was detected on the systematic visit at 48 hours; i.e., was not a result of a complaint from the volunteer nor a consultation to the medical staff, it was not associated with pain or fever. Importantly, there was no contro-lateral reactions at the previous injection site, a phenomenon which has been described with other clinical trials relying on ~~Montanide~~ MONTANIDE®, particularly with the MSP-1 ~~Montanide~~ MONTANIDE® performed by the NIH and that performed by an Australian group in Queensland. All local reactions were spontaneously resolving within 24 hours or a maximum of 48 hours. There was no increase in size of lymph nodes at the axillary site.

Please amend the paragraph beginning on page 38, line 7 as follows:

- The initial 10 micrograms group with ~~Montanide~~ MONTANIDE® remained unchanged: 3 inoculations of 10 micrograms upon each injection: i.e., M10-10-10.
- The original 30 micrograms with ~~Montanide~~ the MONTANIDE® group received the first 2 injections of 30 micrograms and the third one was decreased to 10 micrograms: M30-30-10.
- The original 100 micrograms with ~~Montanide~~ MONTANIDE® was revised with a first injection of 100 micrograms and following injections of 10 micrograms, i.e., M100-10-10.
- The original 300 micrograms with ~~Montanide~~ MONTANIDE® was revised to 3 injections of 20 micrograms: i.e.,: M20-20-20.

Please amend the paragraph beginning on page 39, line 3 as follows:

T-lymphocyte responses were evaluated by proliferation expressed as a stimulation index, and as Interferon-gamma secretion (the secretion of other cytokines was low). The results showed extremely high immunogenicity of the experimental vaccine with proliferative responses which were nearly as high, as the most potent stimulator (the lectin phytohaemagglutinin (PHA)) with very intense responses recorded already at the first month, i.e., after the first immunization as compared with responses obtained at month 0 before the immunization. These high responses remained overall unchanged over the follow-up, i.e., at months 2, 4 and 5, i.e., one month after the third immunization. There was some variation in the intensity of the responses depending on the protocol but, overall, all responses were high and were noticeably as high as using alum as using ~~Montanide~~ MONTANIDE®. The only difference with alum was that responses were somewhat lower after the first injection and

increased after the second one, whereas they were maximal from ~~form~~ the first injection when using ~~Montanide~~ MONTANIDE®, and remained high.

Please amend the paragraph beginning on page 39, line 20 as follows:

Similarly, IFN-gamma secretion in response to the LSP peptide were extremely high, in the range of 10 000 to 50 000 International Units, nearly as high as those induced by the potent stimulator PHA or Tetanus Toxoid (TT). They were already maximal after the first immunization and remained high over all of the immunization process with the same phenomenon of a slight increase from first to second injection with alum which was not seen with ~~Montanide~~ MONTANIDE®, i.e., a more progressive response obtained with alum.

Please amend the paragraph beginning on page 42, line 3 as follows:

In total, the study of immune responses showed a very satisfactory, overall immunogenicity with extremely high T-cell responses, somewhat lower antibody responses with variations in the ability to recognize the native protein. The overall immunogenicity was much higher than that recorded in pre-clinical models employed before, i.e., in mice and in South-American primates where responses with ~~Montanide~~ MONTANIDE® were lower and the responses with alum were absent. This improvement in immunogenicity in humans as compared to the models is dependent on the selection of the LSP sequence based on studies made in humans and not in the models where the most relevant T-cell epitopes and B-cell epitopes have been selected by studies of the existing responses in individuals exposed to malaria under field conditions. The LSP associated 3 major T-cell epitopes in those populations and 3 major B-cell epitopes in those populations. The results lend support to the

strategy by showing higher level of responses using this combination of human epitopes in humans as compared to models.

Please amend the paragraph beginning on page 44, line 10 as follows:

These results are better in terms of safety than those recorded previously using either MSP-1 1.19 alum or MSP-1 and MSP-2 combinations with ~~Montanide~~ MONTANIDE®, where severe contro-lateral effects on the previous injection sites and generalized reactions with fever were recorded.

Please delete the original Abstract appearing on page 52 of the present application and insert therefor the enclosed substitute Abstract.